

```

$PROBLEM AN EXAMPLE INHIBITORY INDIRECT RESPONSE MODEL
;DVID = 0 for dose, 1 for PK, 2 for PD
;CMT = 1 for dose, 2 for PK, 4 for PD
$INPUT ID TIME AMT RATE DV DVID CMT MDV KAI CLI V2I QI V3I PDBASE

$DATA testdata1.csv IGNORE=@ IGNORE=(DVID.EQ.1)

$SUBROUTINES ADVAN13
$MODEL NCOMP=4 COMP=(DEPOT) COMP=(CENTRAL) COMP=(PERIPERAL) COMP=(RESPONSE)
$PK
;PK parameters
  CL = CLI
  V = VI
  KA = KAI
  S2 = V/1000

;PD parameters
  TVEMAX = THETA(1)
  EMAX = TVEMAX*EXP(ETA(1))
  TVEC50 = THETA(6)
  EC50 = TVEC50*EXP(ETA(2))
  TVKIN = THETA(3)
  KIN = TVKIN*EXP(ETA(3))
  TVBASE = THETA(4)
  BASE = TVBASE*EXP(ETA(4))
  KOUT = KIN/BASE
  A_0(4) = BASE ; you could use PDBASE instead of estimated baseline

$DES
DADT(1) = -KA*A(1)
DADT(2) = KA*A(1) - CL/V2*A(2) - Q/V2*A(2) + Q/V3*A(3)
DADT(3) = Q/V2*A(2) - Q/V3*A(3)
CP = A(2)/S2 ;Make sure this uses the scaling factor to be in proper units
EFF = EMAX * (CP/(CP + EC50)) ; you could use a linear effect here if desired
; Use one of the equations below
; Select the equation by removing the semi-colon at the beginning of the line
;DADT(4) = KIN * (1 - EFF) - KOUT*A(4) ; use this for inhibition of production
;DADT(4) = KIN - KOUT * (1 + EFF) * A(4) ; use this for stimulation of elimination

$ERROR
IPRED = F
FLAG = 0
IF(CMT.EQ.4) FLAG=1
Y = IPRED + FLAG*ERR(1)

$THETA
10 ;EMAX
0.3 ;EC50
0.1 ;KIN
80 ;BASE
$OMEGA
0.05 ;IIV EMAX
0.05 ;IIV EC50
0 FIX ;IIV KIN
0.1 ;IIV BASE
$SIGMA
0.2 ;RUVADDEFF - residual PD error

```